

### Remarks

Claims 4, 54 and 78 are amended. Claims 1-109 are pending.

Support for the amendment to claims 4 and 54 is found, for instance, in formulas XXV-XXVI.

Support for the amendment to claim 78 is found in originally-filed claim 78.

In response to the Restriction Requirement mailed June 2, 2005, Applicants provisionally elect, with traverse, the invention of claims 2-12, 15 and 107-109 (Group I), directed to a compound of formula (I): R-linker-A-X, wherein R is one or more functional groups, wherein the linker is a multiatom straight or branched chain including C, N, S, or O, wherein A-X is a substrate for a dehalogenase, wherein X is a halogen, and wherein at least one functional group is an amino acid, protein, glycoprotein, nucleic acid molecule, drug, lipid, biotin, or solid support, and methods of making the compound. With regard to the election of a specie from one of the functional groups recited in claim 10 and from one of the functional groups in claim 15, Applicant provisionally elects, with traverse, the specie biotin (recited in claim 10) and the specie chromophore (recited in claim 15). Applicant believes claims 1-10 and 107-109 read on the elected specie biotin and claims 1-9, 11, 15, and 107-109 read on the elected specie chromophore. Reconsideration and withdrawal of the Restriction Requirement and the election of species, in view of the remarks below, is respectfully requested.

The Restriction Requirement is traversed on the basis that the inventions are closely related. That is, claims directed to a dehalogenase substrate having formula (I): R-linker-A-X, wherein R is one or more functional groups, and wherein at least one functional group is an amino acid, protein, glycoprotein, nucleic acid molecule, drug, lipid, biotin, or solid support, and methods of making the compound (claims 2-12, 15 and 107-109; Group I) are clearly related to claims directed to a dehalogenase substrate having formula (I): R-linker-A-X, wherein R is one or more functional groups, and wherein at least one functional group is a fluorophore recited in claim 13, and methods of making the compound (claims 2-9, 11-13, 15, and 107-109; Group II), claims directed to a dehalogenase substrate having formula (I): R-linker-A-X, wherein R comprises two functional groups (claims 2-9, 11-12, 14-15, and 107-109; Group III), claims directed to a compound of formula (II)-(XXVII), compounds which fall within the

scope of formula (I), and methods of making those compounds (claims 78 and 107-109; each formulae corresponding to one of Groups XIII-XXXVIII), claims directed to methods of using a hydrolase substrate, such as a dehalogenase substrate, to detect a mutant hydrolase which is capable of forming a bond with a hydrolase substrate having at least one functional group, wherein the mutant hydrolase has at least one substitution at an amino acid residue in the corresponding wild-type hydrolase that is associated with activating a water molecule which cleaves the bond formed between the corresponding wild-type hydrolase and hydrolase substrate (claims 35-37 and 52-66; Group VII), claims directed to methods of using a hydrolase substrate, such as a dehalogenase substrate, to detect a mutant hydrolase which forms a bond with a hydrolase substrate which comprises at least one functional group, wherein the mutant hydrolase has at least one amino acid substitution at an amino acid residue in the corresponding wild-type hydrolase that forms an ester intermediate with the substrate (claims 35, 38-39, and 52-66; Group VIII), claims directed to methods of using a hydrolase substrate, such as a dehalogenase substrate, to isolate a molecule, cell or subcellular organelle of interest, which employ a mutant hydrolase which is capable of forming a bond with a hydrolase substrate having at least one functional group, wherein the mutant hydrolase has at least one substitution at an amino acid residue in the corresponding wild-type hydrolase that is associated with activating a water molecule which cleaves the bond formed between the corresponding wild-type hydrolase and hydrolase substrate (claims 40-42, 45-46, and 52-66; Group IX), claims directed to methods of using a hydrolase substrate, such as a dehalogenase substrate, to isolate a molecule, cell or subcellular organelle of interest, which employs a mutant hydrolase which forms a bond with a hydrolase substrate which comprises at least one functional group, wherein the mutant hydrolase has at least one amino acid substitution at an amino acid residue in the corresponding wild-type hydrolase that forms an ester intermediate with the substrate (claims 40, 43-46 and 52-66; Group X), claims directed to a methods to label a cell which employ a hydrolase substrate, e.g., a dehalogenase substrate, and a mutant hydrolase which is capable of forming a bond with a hydrolase substrate with at least one functional group, wherein the mutant hydrolase has at least one substitution at an amino acid residue in the corresponding wild-type hydrolase that is associated with activating a water molecule which cleaves the bond formed between the

corresponding wild-type hydrolase and hydrolase substrate (claims 47-49, 52-68, 71-77, and 91-96; Group XI), and claims directed to methods to label a cell which employ a hydrolase substrate, e.g., a dehalogenase substrate, and a mutant hydrolase which is capable of forming a bond with a hydrolase substrate with at least one functional group, wherein the mutant hydrolase has a substitution at an amino acid residue in the corresponding wild-type hydrolase that forms an ester intermediate with the substrate (claims 47, 50-77, 91-96; Group XII). Thus, claims directed to dehalogenase substrates having at least one functional group and to methods of using hydrolase substrates with at least one functional group are related.

The Restriction Requirement is also traversed on the basis that Restriction Requirements are optional in all cases. M.P.E.P. § 803. If the search and examination of at least a portion of an entire application can be made without serious burden, the Examiner must examine it on the merits, even though it arguably may include claims to distinct or independent inventions. M.P.E.P. § 803. Moreover, it is submitted that Applicants should not be required to incur the additional costs associated with the filing of multiple divisional applications in order to obtain protection for the claimed subject matter, e.g., filing 40 divisional applications. Due to the relatedness of the subject matter of at least the claims in Group I and Groups II-III, VII-XXXVIII), those Groups can be efficiently and effectively searched in a single search with no additional burden placed on the Examiner. In particular, the claims in Group I and Groups II-III can be efficiently and effectively searched in a single search with no additional burden placed on the Examiner, as the claims in those Groups are in the same class (532) and subclass (517) for search purposes.

Moreover, as acknowledged by the Examiner, claim 1 links the inventions of Groups I-III. Therefore, the claims in those Groups should be examined in the same application. M.P.E.P. § 809.03.

Thus, the Restriction Requirement is properly traversed. Accordingly, reconsideration and withdrawal of the Restriction Requirement is respectfully requested.

Further, Applicants' Representatives respectfully request rejoinder of the claims in Groups VII-XII (methods of using a hydrolase substrate with at least one functional group) with the claims in Group I, upon a notice of allowable subject matter for the claims in Group I.

The requirement to elect a species is traversed on the basis that the disclosed species have a disclosed relationship, i.e., they are molecules which can be attached to a hydrolase substrate, e.g., a dehalogenase substrate, and render that substrate readily detectable. Therefore, withdrawal of the species election is respectfully requested.

Conclusion

Applicants respectfully submit that the claims are in condition for allowance and notification to that effect is earnestly requested. The Examiner is invited to telephone Applicants' attorney at (612) 373-6959 to facilitate prosecution of this application.

If necessary, please charge any additional fees or credit overpayment to Deposit Account No. 19-0743

Respectfully submitted,

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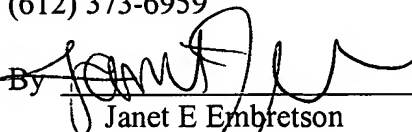
By their Representatives,

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Date

August 5, 2005

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**CERTIFICATE UNDER 37 CFR 1.8:** The undersigned hereby certifies that this correspondence is being deposited with the United States Postal Service with sufficient postage as first class mail, in an envelope addressed to: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450 on this 5 day of August, 2005.

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